

Listing of Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Claims 1-32 (cancelled).

Claim 33 (currently amended): ~~The A screening method according to claim 32 for the identification of agents which modulate initiation of DNA replication wherein said method comprises detecting or measuring the effect of an agent on a nucleic acid molecule selected from the group consisting of:~~

- a) a nucleic acid molecule comprising a nucleic acid sequence represented in any of SEQ ID NO: 45, 46, 66, 67, 68, 69, 70, 71, 72 or 73;
- b) a nucleic acid molecule which hybridizes to the nucleic acid sequence in (a) and which has Ciz1 activity or activity of a variant thereof;
- c) a nucleic acid molecule which has a nucleic acid sequence which is degenerate because of the genetic code to a sequence in a) or b);
- d) a nucleic acid molecule which has a nucleic acid sequence that is at least 95% identical to the nucleic acid sequence in (a) and which has Ciz1 activity; and
- e) a nucleic acid molecule derived from the genomic sequence at the Ciz1 locus or a nucleic acid molecule that hybridizes to the genomic sequence.

Claim 34 (cancelled).

Claim 35 (currently amended): The screening method according to claim 32 33, wherein said method comprises one or more of the following steps:

(i) forming a preparation comprising a candidate agent to be tested and a polypeptide molecule, ~~or an active fragment thereof~~, encoded by a nucleic acid molecule selected from the group consisting of:

- a) a nucleic acid molecule comprising a nucleic acid sequence represented in any of SEQ ID NO: 45, 46, 66, 67, 68, 69, 70, 71, 72 or 73; and
- b) a nucleic acid molecule which hybridizes to the nucleic acid sequence in (a) and which has Ciz1 activity or activity of a variant thereof;

- e) b) a nucleic acid molecule which has a nucleic acid sequence which is degenerate because of the genetic code to the sequences in a) ~~and b)~~ and encodes a polypeptide with DNA initiation activity;
- d) ~~a nucleic acid molecule which has a nucleic acid sequence that is at least 95% identical to the nucleic acid sequence in (a) and which has Ciz1 activity; and~~
- e) ~~a nucleic acid molecule derived from the genomic sequence at the Ciz1 locus or a nucleic acid molecule that hybridises to the genomic sequence; and~~

(ii) detecting or measuring the effect of the agent on the activity of said polypeptide.

Claim 36 (cancelled).

Claim 37 (currently amended): The method according to claim 32 33 wherein said screening method is a cell-based screening method.

Claim 38 (previously presented): The method according to claim 37 wherein the cell naturally expresses the Ciz1 polypeptide.

Claim 39 (currently amended): The method according to claim 37 wherein the cell is transfected with a nucleic acid molecule encoding Ciz 1 or a fragment or splice variant thereof.

Claims 40-50 (cancelled).

Claim 51 (currently amended): A diagnostic method for the identification of proliferative disorders a cancer comprising detecting the presence or expression of the Ciz 1 gene, Ciz1 splice variants and mutations in the genomic or protein sequence thereof.

Claim 52 (currently amended): A The diagnostic method according to claim 51 wherein said method comprises one or more of the following steps:

(i) contacting a sample isolated from a subject to be tested with an agent which specifically binds a ~~polypeptide with Ciz 1 activity or a nucleic acid molecule~~

comprising a nucleic acid sequence as represented by SEQ ID NO: 45, 46, 66, 67, 68, 69, 70, 71, 72 or 73 and encoding a polypeptide with Ciz 1 DNA initiation activity;

- (ii) detecting or measuring the binding of the agent on said ~~polypeptide~~ or nucleic acid in said sample;
- (iii) measuring expression levels of Ciz1 and Ciz1 isoform using reverse-transcribed PCR or real-time PCR;
- (iv) measuring the presence of nucleic acid ~~or amino-acid~~ mutations based on altered conformational properties of the molecule; and
- (v) sequence determination.

Claims 53-64 (cancelled)

Claim 65 (currently amended): A kit comprising ~~Ciz 1 nucleotide or polypeptide sequence, or any fragment or variant thereof~~ primers selected from the group consisting of SEQ ID NO: 17-25 which binds bind to Ciz 1 alternate splice variants.

Claim 66 (new): The method according to claim 35 wherein said screening method is a cell-based screening method.

Claim 67 (new): The method according to claim 66 wherein the cell naturally expresses the Ciz1 polypeptide.

Claim 68 (currently amended): The method according to claim 66 wherein the cell is transfected with a nucleic acid molecule encoding Ciz 1 or a fragment or splice variant thereof.

Claim 69 (new): The method according to claim 52 wherein the cancer is a pediatric cancer selected from the group consisting of: retinoblastoma, neuroblastoma, Burkett lymphoma, medulloblastoma, and Ewings Sarcoma family tumors.

Claim 70 (new): The method according to claim 52 wherein the cancer is carcinoma, adenocarcinoma, lymphoma or leukemia.

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Claim 71 (new): The method according to claim 52 wherein the cancer is liver, lung or skin cancer.